IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Pastan et al.

Application No. 09/763,393

Filed: July 30, 2001

Confirmation No. 5265

For: PAGE-4, AN X-LINKED GAGE-LIKE GENE EXPRESSED IN NORMAL AND NEOPLASTIC PROSTATE, TESTIS AND UTERUS, AND USES THEREFOR

Examiner: Minh-Tam Davis

Art Unit: 1642

Attorney Reference No. 4239-61541-01

CERTIFICATE OF MAILING

I hereby certify that this paper and the documents referred to as being attached or enclosed herewith are being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: MAIL STOP AMENDMENT COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450 on the date shown below.

Attorney or Agent for Applicant(s)

Date Mailed March 13, 2006

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DECLARATION UNDER 37 C.F.R. §1.131

We, Ira Pastan, Ulrich Brinkman, George Vasmatzis, and Byungkook Lee hereby declare as follows:

1. We are named as co-inventors on the above-referenced application, which is a § 371 U.S. national stage of PCT US99/20046 filed August 31, 1999, which was published in English under PCT Article 21(2), which in turn claims the benefit of U.S. Provisional Application 60/098,993 filed September 1, 1998. The Government of the United States of America as represented by the Secretary of the Department of Health and Human Services is the assignee of the above-referenced application.

2. It is our understanding that pending claims 1-2, 53 and 55 of the above-referenced application have been rejected by the U.S. Patent and Trademark Office for allegedly lacking novelty in view of SEQ ID NO: 2 and pharmaceutical compositions including SEQ ID NO: 2, which is disclosed published in U.S. Patent Application Publication No. 2004/0248256A1. The rejection is asserted under 35 U.S.C. § 102(e), as the Office action states that the Patent Office has preformed a

sequence search and determined that SEQ ID NO: 2 is also disclosed parent U.S. Provisional Application No. 60/084564, which was filed on May 7, 1998.

3. As the named co-inventors of the subject matter described in claims 1-2, 53 and 55, this declaration is presented to demonstrate that the claimed amino acid sequence and fragments thereof were obtained prior to May 7, 1998.

4. Prior to May 7, 1998, we performed a computer analysis of expressed sequence tag (EST) sequences using the National Center for Biotechnology Information (NCBI) dbEST/CGAP database. (See, for example, Adams *et al. Science* **252**, 1651-1656, 1991.) The ESTs from human tissues and tumors were downloaded from ftp://ncbi.nlm.nih.gov/repository/dbEST. The cDNA libraries that we processed are listed in http://www.nci.nlm.nih.gov/UniGene/Hs.Home.html; http://www-bio.llnl.gov/bbrp/image/humlib_info.html; http://genome. wustl.edu/est/est_protocols/ libraries.html; http://inhouse.ncbi.nlm.nih.gov/cgi-bin/ UniGene/lbrowse?org=Hs&OTP=cgap. This approach was designed to be used, in combination with experimental verification, to identify genes that are preferentially expressed in the prostate, in order to identify genes that were targets for the diagnosis or therapy of prostate cancer.

The EST sequences were clustered and sorted as described in the literature (see, for example, Vasmatzis et al., *Proc. Natl. Acad. Sci. USA* **95**, 300-304, 1998). The output of the database analysis is a list of clones that occur frequently in prostate and prostate cancer, as well as in other tumors, and that may also be present in some normal tissues. This list was sorted according to EST frequency in prostate and prostate tumors. Since the EST frequency in libraries of defined tissues approximately correlates with the level of tissue-specific expression of the corresponding gene, this tissue-specific ranking can be used to identify genes that are preferentially expressed in prostate and prostate cancer. One of the cDNA clusters present on the database search list was observed to be preferentially present in prostate and prostate tumor libraries, and additionally, in placenta and in a mixed pooled library that contained mRNA from uterus. This cluster, called Cluster41, was identified to be of interest prior to May 7, 1998.

A printed copy of the directory of files from the database analysis, with dates redacted, is attached as Exhibit A. This directory includes all of the overlapping regions of ESTs used to identify a nucleic acid sequence which encodes SEQ ID NO: 2. The 41st file in the directory is

nh32c06.s1, which is the full-length nucleic acid sequence encoding SEQ ID NO: 2. A sequence comparison is included in these files.

A printout showing the information included in the directory is shown as Exhibit B. Part I of Exhibit B shows the overlapping regions of each EST listed in the directory, each of which is labeled by the name of the EST and the tissue from which it was isolated. Part II of Exhibit B is the full length nucleic acid sequence encoding SEQ ID NO: 2 (a printout from the nh32c06.s1 file). Part III of Exhibit B shows the translation of the full length sequence of nh32c06.s1 and an alignment with the GAGE-6 protein sequence. The nucleic acid sequence has a 5'-untranslated region, and the coding sequence starts from the first ATG (which is translated into methionine) in the amino acid sequence. The N-terminal portion was identified to start as "MSARVRSRSR...." which can be seen in the first line of the nh32c06 translation.

Thus, the amino acid sequence set forth as SEQ ID NO: 2 was identified prior to May 7, 1998. This sequence was identified specifically to use in diagnostic and immunogenic methods.

5. All statements made herein and of our own knowledge are true and all statements made on information are believed to be true; and further, these statements were made with the knowledge that willful false statements and like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statements made may jeopardize the validity of the application or any patent issuing thereon.

Date 3/10/06 Byungkook Lee

Byungkook Lee

Date 3/10/06 Ira Pastan

Ira Pastan

Date _____ George Vasmatzis

George Vasmatzis

Date _____ Ulrich Brinkmann

Ulrich Brinkmann

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Date _____ _____
Byungkook Lee

Date _____ _____
Ira Pastan

Date _____ _____
George Vasmatzis

Date March 05 /06 _____
Ulrich Brinkmann

EXHIBIT A: DIRECTORY PRINTOUT

directory called /glad_d2/sathya/vasm_bck/kiwi/vasm/Work/Prostate5/Cluster41

<<begin>>
-rw-r--r-- 1 sathya user 34998 [DATE REDACTED] seq.log
-rw-r--r-- 1 sathya user 2621 [DATE REDACTED] comp1.align.log
-rw-r--r-- 1 sathya user 1610 [DATE REDACTED] align.log
-rw-r--r-- 1 sathya user [DATE REDACTED] fileout
-rw-r--r-- 1 sathya user 2016 [DATE REDACTED] info.log
-rw-r--r-- 1 sathya user 533 [DATE REDACTED] junk
-rw-r--r-- 1 sathya user 10477 [DATE REDACTED] est.comp1
-rw-r--r-- 1 sathya user 252 [DATE REDACTED] estclnm
-rw-r--r-- 1 sathya user 252 [DATE REDACTED] estleft
-rw-r--r-- 1 sathya user 650 [DATE REDACTED] tempt
-rw-r--r-- 1 sathya user 385 [DATE REDACTED] za22c07.r1
-rw-r--r-- 1 sathya user 258 [DATE REDACTED] EST80996
-rw-r--r-- 1 sathya user 58 [DATE REDACTED] temp
-rw-r--r-- 1 sathya user 514 [DATE REDACTED] yi82c07.s1
-rw-r--r-- 1 sathya user 366 [DATE REDACTED] C18137
-rw-r--r-- 1 sathya user 387 [DATE REDACTED] EST81031
-rw-r--r-- 1 sathya user 445 [DATE REDACTED] C18969
-rw-r--r-- 1 sathya user 562 [DATE REDACTED] yi82c07.r1
-rw-r--r-- 1 sathya user 419 [DATE REDACTED] aa07e08.s1
-rw-r--r-- 1 sathya user 469 [DATE REDACTED] zr65g11.s1
-rw-r--r-- 1 sathya user 531 [DATE REDACTED] yw73c12.s1
-rw-r--r-- 1 sathya user 538 [DATE REDACTED] yw73c12.r1
-rw-r--r-- 1 sathya user 518 [DATE REDACTED] zr65g11.r1
-rw-r--r-- 1 sathya user 1920 [DATE REDACTED] comp1.lst
-rw-r--r-- 1 sathya user 252 [DATE REDACTED] comp1.lst2
-rw-r--r-- 1 sathya user 533 [DATE REDACTED] comp1.seq
-rw-r--r-- 1 sathya user 1004 [DATE REDACTED] align.keep
-rw-r--r-- 1 sathya user 149 [DATE REDACTED] comp_ests.1
-rw-r--r-- 1 sathya user 533 [DATE REDACTED] compseq.1
-rw-r--r-- 1 sathya user 5085 [DATE REDACTED] est_cl
-rw-r--r-- 1 sathya user 265 [DATE REDACTED] nf19h11.s1
-rw-r--r-- 1 sathya user 257 [DATE REDACTED] nr35f03.s1
-rw-r--r-- 1 sathya user 320 [DATE REDACTED] nh24a11.s1
-rw-r--r-- 1 sathya user 397 [DATE REDACTED] nc79f08.s1
-rw-r--r-- 1 sathya user 390 [DATE REDACTED] nc33g02.r1
-rw-r--r-- 1 sathya user 453 [DATE REDACTED] nc79f08.r1
-rw-r--r-- 1 sathya user 495 [DATE REDACTED] nt72b09.s1
-rw-r--r-- 1 sathya user 470 [DATE REDACTED] nh24e10.s1
-rw-r--r-- 1 sathya user 477 [DATE REDACTED] nc33g02.s1
-rw-r--r-- 1 sathya user 460 [DATE REDACTED] nt78f01.s1
-rw-r--r-- 1 sathya user 563 [DATE REDACTED] nh32c06.s1
-rw-r--r-- 1 sathya user 538 [DATE REDACTED] nc27g01.r1
<<end>>

EXHIBIT B: CONTENT OF THE SECOND FILE IN ABOVE DIRECTORY

<<begin>>
PART I.
C-prost-placenta...
nh32c06.s1 comp1 ----------> prost.tu
zr65g11.r1 comp1 ---------->.. poole.xx
nt72b09.s1 comp1 x---------->.. prost.tu
yw73c12.r1 comp1 .---------->. place.in
-yw73c12.s1 comp1 .<----------. place.in
-nc33g02.s1 comp1 ...<----------. prost.ca
nh24e10.s1 comp1 ...---------->. prost.no
nc79f08.r1 comp1 .x---------->.... prost.ca
-zr65g11.s1 comp1 ...<----------. poole.xx
nt78f01.s1 comp1 .....x----------> prost.tu
-aa07e08.s1 comp1 .....<----------. poole.xx
yi82c07.r1 comp1 ---------->. place.xx
-nc79f08.s1 comp1 .....<----------x prost.ca
C18969 comp1 ---------->..... place.xx
nc33g02.r1 comp1 ...x---------->..... prost.ca
nc27g01.r1 comp1 .xxxx----------> prost.no
EST81031 comp1 .---------->..... place.xx
C18137 comp1 ..---------->..... place.xx
-yi82c07.s1 comp1 .<----------.. place.xx
nh24a11.s1 comp1 ...---------->..... prost.no
nf19h11.s1 comp1 .---------->..... prost.no
EST80996 comp1 .---------->..... place.xx
-nr35f03.s1 comp1 .....<----------. prost.no
-za22c07.r1 comp1 .....<xxxxxxxxx-------. livsp.ft

PART II
AA524997 nh32c06.s1 918 @NCI_CGAP_Pr3@ @Homo sapiens@ @
GGTCGACCTTCGCCAGGCTCTCTGCTGACTCAAGTTCTTCAGTTCACGATCTTCTAGTTGCAG
CGATGAG
TGCACGAGTGAGATCAAGATCCAGAGGAAGAGGAGATGGTCAGGAGGCTCCCGATGTGGTT
GCATTCGTG
GCTCCCGGTGAATCTCAGCAAGAGGAACCACCAACTGACAATCAGGATATTGAACCTGGAC
AAGAGAGAG
AAGGAACACCTCCGATCGAAGAACGTAAAGTAGAAGGTGATTGCCAGGAAATGGATCTGGA
AAAGACTCG
GAGTGAGCGTGGAGATGGCTCTGATGTAAAAGAGAAGACTCCACCTAATCCTAAGCATGCT
AAGACTAAA
GAAGCAGGAGATGGGCAGCCATAAGTTAAAAAGAAGACAAGCTGAAGCTACACACATGGC
TGATGTCACA
TTGGAAATGTGACTGAAAATTTGGAAATTCTCTCAATAGAGTCTGAGTTTTCTCTGAAGAAA
AAAAAAAA
A
PART III

```
Gage-6          MSWRGRSTYYWPRPRRYVQPPEVIGPMRPEQFSDEVEPATPEEGEPATQRQDPAAAQ
nh32c06 STFARLSADSSSSVHDLLVAAMSARVRSRSRGRGDGQEAPDVVAFVAPGESQQEEPPTDNQDIEP
```

```
Gage-6   EGEDEGASAGQGPKPEADSQEQGHPQTGCECEDGPDGQEVDPPNPEEVKTPEEGEKQSQC
           E EG     +   K E D QE     +T   E   DG D +E   PPNP+  KT E G+ Q
nh32c06 GQEREGTPPIEERKVEGDCQEMDLEKTRSERGDGSDVKEKTPPNPKHAKTKEAGDGQP
```

<<end>>